

Amendments to the Specification:

Please replace the paragraph beginning on page 8, line 18 through page 9, line 16 with the following amended paragraph:

--The virus can be replication competent (e.g., completely wild-type or essentially wild-type such as Ad d1309 or Ad d1520), conditionally replicating (designed to replicate under certain conditions) or replication deficient (substantially incapable of replication in the absence of a cell line capable of complementing the deleted functions). Alternatively, the viral genome can possess certain modifications to the viral genome to enhance certain desirable properties such as tissue selectivity. For example, deletions in the E1a region of adenovirus result in preferential replication and improved replication in tumor cells. The viral genome can also be modified to include therapeutic transgenes (as more fully described below). The virus can possess certain modifications to make it "selectively replicating," i.e. that it replicates preferentially in certain cell types or phenotypic cell states, e.g., cancerous. For example, a tumor or tissue specific promoter element can be used to drive expression of early viral genes resulting in a virus which preferentially replicates only in certain cell types. Alternatively, one can employ a pathway-selective promoter active in a normal cell to drive expression of a repressor of viral replication. For example, a conditionally replicating adenoviral vector can be created by the use of a promoter active in the presence of endogenous p53 to drive expression of the E2F-Rb fusion protein (a potent inhibitor of the E2 adenoviral promoter). In such instances, where there is a defect in the p53 pathway such that active p53 is not present (e.g., a tumor cell), the repressor of viral replication is not expressed and the virus will replicate. However, where p53 is present (e.g. normal cells) the repressor of viral replication is expressed and viral replication is prevented. Selectively replicating adenoviral vectors that replicate preferentially in rapidly dividing cells are described in International Patent Application No. WO1999US0021451 (Publ. No. WO 00/22136) entitled "Recombinant E1A Deleted Adenoviral Vectors." These vectors contain modifications to the E1a coding sequence so as to produce E1a gene products that are deficient in binding to one or more E1a p300 protein family members and one or more Rb protein family members, but retain the transactivating function of the E1a CR3 domain.

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PATENT

Selectively replicating viruses are also described in International Patent Application No. WO1999US0021452 (Publ. No. WO 00/22137), which is entitled "Selectively Replicating Viral Vectors." These viral vectors replicate in cells that have a defective pathway (e.g., a p53 or TGF-beta pathway), but not in cells with an active pathway.--